ORIGINAL CONTRIBUTION

Clinical Analysis of the Related Factors in Acute Appendicitis

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Background: In order to determine reliable clues for early diagnosis of acute appendicitis, this study was conducted to examine the related factors in patients with clinically suspected acute appendicitis.

Methods: We retrospectively analyzed 282 patients with the clinical diagnosis of acute appendicitis at China Medical College Hospital in Taiwan from January to December 2000. To study the significant related factors of acute appendicitis, the t-test, chi-square analysis, and multivariate logistic regression analysis were used.

Results: There were 153 males (54.3 percent) and 129 females (45.7 percent). The mean age was 30.3 ± 17.4 years (range 1 to 81). The diagnostic rate of acute appendicitis was 86.2 percent . If the combination of elevated C-reactive protein, leukocytosis and elevated neutrophil ratio was used, satisfactory specificity and positive predictive value were achieved in diagnosing acute appendicitis. After controlling for the other covariates, the multivariate logistic regression analysis showed that the significant related factors of acute appendicitis were male sex (odds ratio = 3.4; 95 percent confidence interval = 1.6 to 7.3; p <0.01) and elevated neutrophil ratio (odds ratio = 4.6; 95 percent confidence interval = 2.0 to 10.6; p <0.001).

Conclusions: If an elevated neutrophil ratio was observed, the probability of acute appendicitis was increased in patients with clinically suspected acute appendicitis. Thus, neutrophil ratio appears to be a good parameter for diagnosis of acute appendicitis in primary healthcare settings.

INTRODUCTION

Acute appendicitis is one of the most common problems requiring emergency surgery [1]. It has been estimated that the accuracy of the clinical diagnosis of acute appendicitis is only between 76 percent and 92 percent [1-5]. Thus, accurate diagnosis of acute appendicitis is still difficult. Delay in diagnosis leads to increased rates of morbidity and mortality [2-3]. It is estimated that 11.2 to 30 percent of acute appendicitis patients suffer intestinal per-

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[d]*Abbreviations*: CRP, c-reactive protein; NR, neutrophil ratio; WBC, white blood cell.

foration due to diagnostic delay [1, 6]. On the other hand, the negative rate of appendectomy varies from 15 to 30 percent [1, 7], but it may lead to postoperative complications, such as adhesion [8-10] and results in socio-economic consequences in form of lost working days and reduced productivity [4]. Thus, improving the diagnosis of acute appendicitis in order to prevent unneeded surgery is a critical topic that has been debated often and vigorously. The use of laparoscopy, ultrasonography, barium enema examination, and computed tomographic scanning has improved diagnostic accuracy [2-3, 8, 11], but these diagnostic approaches are difficult to apply in primary healthcare settings.

Some basic laboratory examinations have been suggested as aids in the diagnosis of acute appendicitis. C-reactive protein (CRP)^d, white blood cell counts (WBC) and differential counts are sensitive markers of inflammatory processes [12-14]. These markers can be easily measured in primary healthcare settings. However, the diagnostic role of these inflammatory markers in acute appendicitis remains equivocal [8-12, 15]. Though inflammatory markers have been discussed previously in other counties, up to now only scant studies have been reported about the association between acute appendicitis and these inflammatory markers in Taiwan. To extend these studies to the health status of people in our country and to help primary care physicians find reliable clues to accurately diagnoses acute appendicitis and thus avoid unnecessary surgery, this study was conducted to examine the related factors in patients with clinically suspected acute appendicitis.

SUBJECTS AND METHODS

From January to December 2000, we retrospectively analyzed the medical records of all appendectomy patients with clinically suspected acute appendicitis at China Medical College Hospital, one medical center in Taichung City, Taiwan. The diagnosis of acute appendicitis was confirmed by histological examination in every case. A total of 282 patients was included in this study. Body temperature was measured by infrared aural thermometer (Genius, Sherwood, St. Louis, Missouri) and in our hospital fever was defined as a aural temperature greater than 37°C. Blood samples were collected for determination of CRP, WBC and differential counts. CRP was measured by nephelometric immunoassay (Beckman Coulter, Inc., Fullerton, California) and in our hospital elevated CRP was defined as serum CRP value greater than 0.8 mg/dl. WBC and differential counts were examined by an automatic cell counter (Cell-Dyn®, 3500R System, Abbott Park, USA). In our hospital leukocytosis was defined as WBC greater than 11,000/mm³ and elevated neutrophil ratio (NR) was defined as a ratio of neutrophils to total white blood cells exceeding 80 percent. The statistical analyses were performed with the aid of a SAS software package (Version 6.12, SAS Institute, Inc., Cary, North Carolina). The methods of statistical analysis were the t-test, chi-square analysis, and multivariate logistic regression analysis. Statistical significance was defined as differences associated with a p-value less than 0.05.

RESULTS

There were 153 males (54.3 percent) and 129 females (45.7 percent). The mean age was 30.3 ± 17.4 years (range 1 to 81). Histologic examination demonstrated 39 cases of normal appendix (13.8 percent), 211 cases of simple acute appendicitis and 32 cases of acute appendicitis with perforation. Thus, the diagnostic rate of acute appendicitis was 86.2 percent. The characteristics of laboratory data are shown in Table 1. Subjects with acute appendicitis had higher levels of body temperature,

Table 1. Characteristics of the clinical data.

Variable	Normal	Acute appendicitis	p value
Age (years)	28.3 ± 10.5	30.6 ± 18.3	0.2610
Body temperature (ºC)	36.7 ± 1.0	37.1 ± 1.0	**0.0254**
C-reactive protein (mg/dl)	3.6 ± 5.3	4.9 ± 6.2	0.2238
White blood cell (/mm^3)	12,445 ± 4,079	14,948 ± 4,868	**0.0026**
Neutrophil ratio (percent)	75.4 ± 8.3	80.7 ± 8.7	**0.0004**

WBC and NR (p < .05, p < .01 and p < .001, respectively). The comparisons of the related parameters for acute appendicitis are shown in Table 2. The significant correlates of acute appendicitis by chi-square analysis are sex, leukocytosis, and elevated NR (p < .01). The specificity and positive predictive value of elevated NR in diagnosing appendicitis were 76.9 percent and 94.2 percent, respectively. In contrast, sensitivity was decreased when elevated CRP, leukocytosis, and elevated NR were used together in diagnosing acute appendicitis, but specificity and positive predictive value were increased. The results of multivariate logistic regression analyses for acute appendicitis are shown in Table 3. After controlling for the other covariates, the significantly related factors in acute appendicitis are male sex (odds ratio = 3.4; 95 percent confidence interval = 1.6 to 7.3; p < .01) and elevated NR (odds ratio = 4.6, 95 percent confidence interval = 2.0 to 10.6, p < .001). No significant association was found between acute appendicitis and fever, elevated CRP, or leukocytosis.

DISCUSSION

Diagnosis of acute appendicitis is primarily established by the surgeon's evaluation based on clinical features, such as a detailed medical history and physical examination. Even so, the rate of appendectomy where normal appendices are found remains high, about 15 to 30 percent [1, 7]. Though many diagnostic approaches, such as ultrasonography or computed tomographic scanning, have improved diagnostic accuracy [2-3, 8, 11], their availability in primary healthcare settings

Table 2. Comparisons of the related parameters.

	Sensitivity (percent)	Specificity (percent)	Positive predictive (percent)	Negative predictive (percent)
Fever	32.1	76.9	89.7	15.4
CRP	68.3	35.9	86.9	15.4
WBC	81.9	38.5	89.2	25.4
NR	60.1	76.9	94.2	23.6
CRP + WBC	54.7	61.5	89.9	17.9
CRP + NR	42.4	84.6	94.5	19.1
WBC + NR	53.5	82.1	94.9	22.1
CRP + WBC + NR	37.0	87.2	94.7	18.2

CRP, elevated CRP; WBC, leukocytosis; NR, elevated neutrophil ratio.

Table 3. Multivariate logistic regression analysis of the related factors in acute appendicitis

	Variable	Odds ratio	95% CI
Intercept	0.04 (0.5)		
Gender (female as reference)			
Male	1.2 (0.4)	3.4	**1.6 to 7.3***
Body temperature (≤37ºC as reference)			
>37ºC	0.2 (0.4)	1.3	0.5 to 3.0
C-reactive protein (≤0.8 mg/dl as reference)			
>0.8	0.1 (0.4)	1.1	0.5 to 2.5
White blood cell (≤11,000/mm³ as reference)			
>11,000	0.7 (0.4)	2.0	0.9 to 4.3
Neutrophil ratio (≤80 as reference)			
>80	1.5 (0.4)	4.6	**2.0 to 10.6****

EP, estimated parameter; SE, standard error; OR, odds ratio; CI, confidence interval.
$*p < .01$; $**p < .001$.

and their high cost remain problematic. CRP, WBC, and differential white cell counts have been applied frequently in a variety of diseases worldwide, and such standard tests can be performed in medical centers or in primary care without analytical variability or significant error [12-13, 16]. However, the diagnostic value of these simple procedures in acute appendicitis has been debated by many authors and controversy still exists about which inflammatory markers are relevant to diagnosis of acute appendicitis [5-11, 15]. In our study, multivariate logistic regression did not show a significant association between acute appendicitis and elevated CRP or leukocytosis; only elevated NR was a significantly related factor. That is, when clinical suspicion of acute appendicitis was established, we could check the NR. If an elevated NR was found, the probability of acute appendicitis was significantly increased. Because it is easily measured and its cost is low, the NR is a good parameter for diagnosis of acute appendicitis in primary healthcare settings. In addition, if the combination of elevated CRP, leukocytosis, and elevated NR was used, improved specificity and positive predictive value were obtained in

diagnosing acute appendicitis. There were, however, several limitations and additional questions raised in this study. First, male sex appears to be a risk factor of acute appendicitis. Because of no mention of this association in the previous literature, we are unsure of the nature of this association between sex and acute appendicitis. The cause of this correlation needs additional investigation. Second, patients with other types of abdominal pain also often demonstrated elevated inflammatory markers, which limits their uses in differentiating these problems from acute appendicitis. In such cases, these blood tests yielded both false-positive and false-negative results. It will be important to study another group of patients with other types of abdominal pain who did not undergo appendectomy. Thus, we could compare these two groups to obtain further results. In conclusion, if elevated NR is detected, the probability of acute appendicitis appears to be increased in patients with clinically suspected acute appendicitis. When elevated CRP, leukocytosis, and elevated NR are used together, specificity and positive predictive value are increased in diagnosing acute appendicitis.

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